Cost-effectiveness of 4 empiric antimicrobial regimens in patients with community-acquired pneumonia

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Four empiric antimicrobial regimens used to treat adults with community-acquired pneumonia (CAP) were examined. The regimens were levofloxacin monotherapy (Levo), ceftriaxone monotherapy (CTX), ceftriaxone plus a macrolide (CTX+Mac), and ceftriaxone plus levofloxacin (CTX+Levo).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised CAP patients with PSI Class IV or V. Patients were excluded if they had a history of the human immunodeficiency virus or acquired immunodeficiency syndrome, had been hospitalised within the last 7 days, or were immunocompromised secondary to chemotherapy or solid organ transplant.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from November 1999 to April 2000. The price year was 2005.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out on the same sample of patients as that included in the effectiveness analysis, but it was unclear whether it was performed prospectively or retrospectively.

Study sample
Power calculations were not performed. Patients were identified using the discharge diagnosis code at the authors’ institution. The patients were allocated to the treatment groups on the basis of the antimicrobial received in the first 24 hours of hospitalisation. A total of 415 patients admitted to the institution with the eligible discharge codes were classified as PSI Class IV and V. Of these, 311 patients received one of the four treatments under study and were included in the effectiveness study. There were 151 patients (54% women) in the Levo group, 61 (61% women) in the CTX+Levo group, and so forth.
CTX group, 61 (31% women) in the CTX+Mac group, and 38 (58% women) in the CTX+Levo group. The median age was 82 years (interquartile range, IQR: 76 - 88) in the Levo group, 82 years (IQR: 72 - 89) in the CTX group, 76 years (IQR: 67 - 82) in the CTX+Mac group, and 80 years (IQR: 75 - 85) in the CTX+Levo group.

**Study design**

This was a cohort study that was carried out a single centre, the Baptist Health System and the University of Texas Health Science Center at San Antonio, USA. It appears to have been a retrospective study. The length of follow-up was unclear, although the study lasted for 6 months. No patient was lost to the follow-up assessment.

**Analysis of effectiveness**

The analysis of the clinical study was restricted to the 311 patients who received one of the four treatments under study. The main clinical outcome was the survival rate. At baseline, there were statistically significant differences among the four groups in terms of patient, age, gender, admission from a nursing home, chronic obstructive pulmonary disease and stroke. Patients who received CTX+Mac were significantly younger, with a lower percentage of women and fewer patients admitted from a nursing home, compared with patients who received Levo or CTX. The proportion of patients stratified to risk class V was lowest among those who received CTX+Mac (27%), followed by CTX+Levo (34%), Levo (36%) and CTX (41%), but these differences did not reach statistical significance, (p=0.3936).

**Effectiveness results**

Clinical results for the whole sample were reported.

For example, patients received intravenous antimicrobials for 4 days (range: 3 - 7) and remained hospitalised for 5 days (range: 3 - 7).

The overall in-hospital mortality rate was 7%. It was significantly higher among patients in risk class V compared with those in risk class IV (13% versus 4%; p=0.0006).

The survival rate was 94% with Levo, 87% with CTX, 98% with CTX+Mac, and 95% with CTX+Levo.

**Clinical conclusions**

The effectiveness analysis showed that the highest survival was achieved with CTX+Mac, while CTX monotherapy was the least effective strategy for the treatment of severe CAP.

**Measure of benefits used in the economic analysis**

The summary benefit measure used was the survival rate. This was derived directly from the effectiveness analysis.

**Direct costs**

The analysis of the costs was undertaken from the perspective of the private health care system. It included hospital charges for room and board, respiratory therapy, pharmacy, laboratory, radiology, central supply, emergency room and miscellaneous. The unit costs were not presented separately from the quantities of resources used, although some data on days of hospitalisation were provided. The estimation of costs came from the hospital billing records of patients included in the study. The respiratory department charged the patients per episode of treatment, and the charge included the cost of some respiratory medication but not antibiotics. A cost-to-charge ratio was then applied. Resource use data for the whole sample came from 393 of the 415 patients initially included in the cost-analysis, while resource use for the four treatments came from the 313 patients included in the effectiveness analysis. Discounting was not relevant given the short timeframe of the analysis. All costs were inflated to 2005 values using the Consumer Price Index.

**Statistical analysis of costs**
The costs were presented as median values with 25th - 75th quartiles. The costs were transformed with the natural logarithm function and tested using the Shapiro-Wilk test, to ensure normality for total hospital costs, pharmacy costs and antibiotic costs. A one-way analysis of variance was used to evaluate associations between antimicrobials received and the natural logarithm of total hospital cost.

**Indirect Costs**
The indirect costs were not included in the cost analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
A probabilistic sensitivity analysis was conducted on the cost-effectiveness ratios. The mortality rate was varied by +/-5% according to a normal distribution, while the total hospital cost was fitted to a log-normal distribution and varied over the entire interval. Ranges of values for mortality were based on some published studies.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The overall cost of care for the 393 evaluable patients was $2.5 million, for which the authors' institution was reimbursed $1.9 million for a net loss of $600,000.

The median cost per patient was $4,356 (IQR: 2,772 - 7,294) with Levo, $4,670 (IQR: 3,406 - 7,544) with CTX, $5,173 (IQR: 3,852 - 7,115) with CTX+Mac, and $6,002 (IQR: 3,646 - 9,186) with CTX+Levo.

As expected, patients in risk class V accrued higher total hospital costs (median $5,836, IQR: 3,690 - 8,442)) than patients stratified to risk class IV (median $4,584, IQR: 83,016 - 7,946)). However, the difference did not reach statistical significance. (p=0.1188).

The analysis of the variables associated with increased cost showed that African-Americans accrued higher hospital costs than Latin-Americans or Caucasians, owing to differences in length of hospital stay.

**Synthesis of costs and benefits**
Average and incremental cost-effectiveness ratios (i.e. the cost per life saved) were calculated to combine the costs and benefits of the alternative strategies.

The average cost per life saved was $4,635 with Levo, $5,368 with CTX, $5,278 with CTX+Mac, and $6,317 with CTX+Levo.

The incremental analysis used Levo as the reference regimen (less costly strategy). The incremental cost-effectiveness ratio was $20,409 for CTX+Mac and $164,514 with CTX+Levo. CTX was dominated by Levo.

The results from the sensitivity analysis showed that the average (i.e. median) cost per life saved was $4,781 (IQR: 3,033 - 7,575) with Levo, $5,768 (IQR: 3,682 - 8,967) with CTX, $5,503 (IQR: 3,608 - 8,336) with CTX+Mac, and $6,067 (IQR: 3,929 - 9,465$) with CTX+Levo.

**Authors' conclusions**
Levofloxacin (Levo) was the most cost-effective treatment for hospitalised patients with severe community-acquired
pneumonia (CAP) in the USA.

**CRD COMMENTARY - Selection of comparators**
The rationale for the selection of the comparators was clear. The four most commonly used antimicrobial therapies for adult patients with CAP were compared. Dosages were not reported. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness data were estimated from a cohort study. It was unclear whether the design of the study was prospective or retrospective. The lack of randomisation might have introduced some selection bias. Further, the study groups were not well matched at baseline, thus the impact of confounding factors cannot be ruled out. The evidence came from a single centre, thus caution is required when extrapolating the results of the analysis to other settings. No formal justification for the size of the sample was provided, and power calculations were not reported. Details of the follow-up were not clearly provided. The patients might have been followed-up until hospital discharge, but this was not explicitly stated. These issues tend to limit the internal validity of the analysis. The authors also acknowledged that they did not assess the rate of repeat hospitalisation, which might have been an indicator of the efficacy of the treatments.

**Validity of estimate of measure of benefit**
The use of the percentage of surviving patients as the summary benefit measure was appropriate since it represents a relevant dimension of health for patients with CAP. However, the impact of the interventions on expected survival was not investigated. In addition, aspects related to quality of life were not considered. The authors noted that the use of survival rate was more appropriate than the widely used “rate of success” to define the efficacy of the treatments. However, they also noted that they were unable to determine which deaths were attributable solely to pneumonia.

**Validity of estimate of costs**
The analysis of the costs was consistent with the authors’ stated perspective. For example, patient bills were used as the source of the data. Hospital charges were used to derive the costs, although the use of charges as proxies for costs is controversial. In effect, a cost-to-charge ratio was applied. A breakdown of the cost items was not clearly provided, while details of the unit costs and quantities of resources used were not given. This might limit the possibility of replicating the analysis in other settings. The period during which the costs and resource use data were gathered was reported. Extensive statistical analyses were carried out to deal with the distribution of the costs and to assess the relationship between baseline characteristics and total costs. The price year was given, which means that reflation exercises in other time periods will be possible. The cost estimates were specific to the study setting, but the total costs were varied in the sensitivity analysis.

**Other issues**
The authors reported the results from other studies and highlighted that the main difference between these studies and the current analysis was the randomised design. However, the issue of the generalisability of the results to other settings was not explicitly addressed. The use of a sensitivity analysis does not fully overcome this limitation, given that the costs appear specific to the study institution. The authors concluded that Levo was the most cost-effective strategy on the basis of average cost-effectiveness results, and that it was unclear whether the incremental cost per life saved of CTX+Mac compared with Levo can be considered good value for money. The study referred to patients suffering from severe CAP and this was reflected in the authors’ conclusions.

**Implications of the study**
The study results suggested that patients admitted to the medical floor for Class IV or V CAP should be treated with Levo. The current study supported the recommendation of avoiding CTX+Levo because this regimen is associated with a very large incremental cost compared with Levo.
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Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by CRD

MeSH
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